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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,831	02/28/2006	Shinji Nakade	Q93540	8160
65565	7590	05/21/2009	EXAMINER	
SUGHRUE-265550			DAVIS, ZINNA NORTHINGTON	
2100 PENNSYLVANIA AVE. NW			ART UNIT	PAPER NUMBER
WASHINGTON, DC 20037-3213			1625	
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			05/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,831	NAKADE ET AL.	
	Examiner	Art Unit	
	Zinna Northington Davis	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 March 2009.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-41 is/are pending in the application.
 4a) Of the above claim(s) 4,10,13,14,17,18,22-24,26,36,40 and 41 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-3, 5-7, 11, 12, 15,16, 21, 27-35, and 37-39 is/are rejected.
 7) Claim(s) 8,9,19,20 and 25 is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/28/06;02/26/08</u> . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

1. Claims 1-41 are pending.
2. In the response filed March 20, 2009, Applicants have elected Group I, claims 1-39, without traverse. Applicants also identify the compound Example 29 (3), 1- {[1-methyl-6-(4-phenylbutoxy)-3, 4-dihydro-2-naphthalenyl]methyl} -3-azetidinecarboxylic acid, as the preferred species.
3. Claims 1-3, 5-9, 11, 12, 15, 16, -16, 19-21, 25, 27-35, and 37-39 are drawn to the elected invention.
4. Claims 4, 10, 13, 14, 17, 18, 22-24, 26, 36, 40 and 41 are withdrawn from consideration. These claims have not been canceled.
5. Rejoinder of the method claims will be addressed upon allowance of claimed subject matter.
6. Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).
7. Claims 1-3, 5-9, 11, 12, 15, 16, -16, 19-21, 25, 27-35, and 37-39 are Markush claims which are generic to the elected invention. The Markush type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. See MPEP 803.02.

8. Claims 1-3, 5-9, 11, 12, 15, 16, -16, 19-21, 25, 27-35, and 37-39 are objected on the grounds that the claims are drawn to an improper Markush group. In re Harnisch, 206 USPQ 300, states that a unity of invention exists where compounds included within a Markush group(1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility. In the instant case, the claimed subject matter does not share a substantial structural feature disclosed as being essential to that utility.

9. The requirement for a proper Markush claim is that it includes only substances that in their physical, chemical and physiological characteristics are functionally equivalent. The members of the instant Markush groups possess widely different, physical and chemical properties. The compounds are not considered functionally equivalent and are so diverse that they demonstrate dissimilar and unrelated properties. The mere fact that there is structural similarity in pharmaceutical agents is not in itself reason to render all the embodiments functionally equivalent.

10. The improper Markush groups are R¹, A, B, X, Y, m and n.

11. The elected compound has been examined and found to be allowable.

The search has been extended beyond the elected compound.

12. The examined subject matter is as follows:

A compound of formula I wherein R¹ is a substituent; A is a cyclic group; n is 0 or 1, wherein when n is 0, m is 1; B is a cyclic group; X is a spacer atom; Y is a spacer which forms a ring. Amending the claims to the examined subject matter would overcome the improper Markush rejection.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1, 27, and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making a solvate of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

- a) Determining if any particular substrate would form a solvate would require synthesis of the substrate and subjecting it to recrystallization with a variety of solvents, temperatures, pressures, and humidity. The experimentation is potentially open-ended.
- b) The direction concerning the solvate is found on page 46, which simply states Applicants intent to make them according to known methods.

c) There is no working example of any solvate formed. The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

d) The nature of the invention is chemical synthesis, which involves chemical reactions. e) The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the

formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate.

f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience.

g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18.

h) The breadth of the claims includes all of the thousands of compounds of formula I as well as the presently unknown list of solvents embraced by the term "solvate".

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 refers to claims 1 and 2 which is improper.

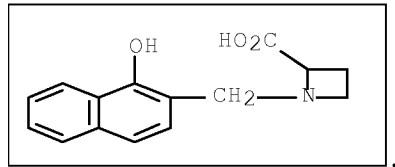
17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3, 5-7, 11, 12, 15, 16, 21, 27-35, and 37-39 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Shen et al. (Reference U, cited by the Examiner).

The instantly claimed compound is disclosed. At page 198, Table 1, see compound 1f. The compound is depicted below:



The claims are fully met when m is 1; R¹ is hydroxyl; A is absent; n is 0; B is a cyclic group, X is a spacer atom; Y is a spacer which forms a ring.

19. The Information Disclosure Statements filed February 28, 2006 and February 26, 2008 have been considered.

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20. Claims 8, 9, 19, 20, and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zinna Northington Davis whose telephone number is 571-272-0682.
22. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300 for regular communications.
23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Zinna Northington Davis/
Zinna Northington Davis
Primary Examiner
Art Unit 1625

Znd
05.13.2009